

CLAIMS

What is claimed is:

1. A spatially defined array of protein expression systems comprising
  - (a) a substrate;
  - (b) a binding surface which covers some or all of the substrate surface; and
  - (c) a plurality of protein expression systems located at discrete positions on portions of said substrate covered by said binding surface.
2. The array of claim 1, wherein said expression systems produce recombinant proteins.
3. The array of claim 2, wherein said proteins produced by said expression systems are immobilized on said array.
4. The array of claim 3, wherein said immobilization of said proteins produced by said expression systems comprises immobilization of said expression systems.
5. The array of claim 3, wherein said immobilization of said proteins produced by said expression systems comprises a direct interaction of said expressed protein with said binding surface.
6. The array of claim 2, wherein said expressed proteins comprise an affinity tag.
7. The array of claim 2, wherein the expressed proteins comprise an epitope tag.
8. The array of claim 1, wherein each discrete position on the array comprises one protein expression system.
9. The array of claim 1, wherein each discrete position on the array comprises a plurality of protein expression system
10. The array of claim 1, wherein each protein expression system expresses a unique protein or peptide.

11. The array of claim 1, wherein at least some of the expression systems express peptides or protein fragments derived from the same protein.

12. The array of claim 1, wherein at least some of the expression systems express related proteins.

5 13. The array of claim 12, wherein said related proteins are related functionally.

14. The array of claim 12, wherein said related proteins are related structurally.

15. The array of claim 1, wherein at least a subset of the proteins expressed by the protein expression systems of the array are members of the same family.

10 16. The array of claim 15, wherein said family of proteins expressed by the protein systems of the array comprises growth factor receptors, hormone receptors, neurotransmitter receptors, catecholamine receptors, amino acid derivative receptors, cytokine receptors, extracellular matrix receptors, antibodies, lectins, cytokines, serpins, proteinases, kinases, phosphatases, ras-like GTPases, hydrolases, steroid hormone receptors, transcription factors, DNA binding proteins, zinc finger proteins, leucine-zipper proteins, homeodomain proteins, intracellular  
15 signal transduction modulators and effectors, apoptosis-related factors, DNA synthesis factors, DNA repair factors, DNA recombination factors, cell-surface antigens, Hepatitis C virus (HCV) proteases, HIC proteases, viral integrases, or proteins from pathogenic bacteria

17. The array of claim 1, further comprising at least 10 discrete locations comprising protein expression systems on one array.

20 18. The array of claim 1, further comprising at least  $10^2$  discrete locations comprising protein expression systems on one array.

19. The array of claim 1, further comprising at least  $10^3$  discrete locations comprising protein expression systems on one array.

20. The array of claim 1, further comprising at least  $10^4$  discrete locations comprising protein expression systems on one array.

21. The array of claim 1, wherein said binding surface comprises a component which binds to said protein expression systems.

5 22. The array of claim 21, wherein the binding surface comprises an antibody which binds to said protein expression systems.

23. The array of claim 1, wherein said binding surface comprises a hydrogel.

24. The array of claim 1, wherein said binding surface comprises a membrane.

25. The array of claim 1, wherein said binding surface comprises at least one functional group that binds to the substrate and at least one functional group that binds to said protein expression systems.

26. The array of claim 1, wherein the binding surface comprises a compound which binds to the proteins produced by said protein expression systems.

27. The array of claim 26, wherein said binding surface comprises an antibody which binds to the proteins produced by said protein expression systems.

28. The array of claim 26, wherein said binding surface comprises at least one layer of coating material.

29. The array of claim 26, wherein said coating comprises a metal film.

30. The array of claim 1, wherein the substrate is selected from the group consisting of

20 silicon, silicon dioxide, alumina, glass, titania, nylon, polypropylene, polyethylene, polystyrene, and acrylamide.

31. A micromachined device comprising the array of protein expression systems of claim 1.

32. A biosensor comprising the array of protein expression systems of claim 1.

33. A method for screening a plurality of proteins for their ability to interact with a component of a sample comprising the steps of:

(a) generating a protein expression array, wherein the array comprises:

(i) a substrate;

(ii) a binding surface which covers some or all of the substrate surface; and

(iii) a plurality of protein expression systems located at discrete positions on portions of the substrate covered by the binding surface; and

(b) detecting either directly or indirectly the interaction of the component with proteins expressed at specific positions comprising the protein expression systems.

34. The method of claim 33, wherein the method comprises detecting the component retained at a specific position on the expression array.

35. The method of claim 33, wherein the method comprises transferring the expressed proteins to known locations on a second array and detecting the interaction of the components of the sample with the second array.

36. The method of claim 33, wherein the step of detection comprises characterization of binding of the components to proteins expressed from protein expression systems located at specific positions on the array.

37. The method of claim 33, wherein the step of detection comprises characterization of an alteration in the activity of proteins expressed from protein expression systems located at specific positions on the array.

38. The method of claim 33, further comprising characterization of DNA isolated from the expression system for which the interaction is detected.

39. The method of claim 33, wherein the component tested for interaction with the proteins expressed by the protein expression systems of the array comprises a protein or peptide.

40. The method of claim 33, wherein the component tested for interaction with the proteins expressed by the protein expression systems of the array comprises a small molecule.

5 41. The method of claim 33, wherein the component tested for interaction with the proteins expressed by the protein expression systems of the array comprises a proprotein.

42. The method of claim 33, wherein the component tested for interaction with the proteins expressed by the protein expression systems of the array comprises a receptor ligand.

10 43. The method of claim 42, wherein the ligand is selected from the group consisting of peptides, peptide mimetics, antibodies, small molecules, natural product extracts, and mixtures of the above.

15 44. The method of claim 33, wherein the interaction of the components of a sample with the expression array is measured by multi-dimensional spectroscopy utilizing ion mobility and time of flight mass spectroscopy for the detection of biological or chemical products formed as the result of the interaction of at least one component of the sample with proteins expressed from specific sites on the protein expression array.

45. The method of claim 44, comprising the steps of:

20 (a) recovering at least a portion of said biological or chemical products formed as the result of the interaction of components of a sample with proteins expressed from specific sites on the protein expression array as an electrospray;

(b) directing the electrospray to an ion mobility chamber which separates the constituents of the directed electrospray based on size, ionic charge, and shape; and

(c) analyzing the separated constituents of the directed electrospray which emerge from the ion chamber by time-of-flight spectroscopy.

46. The method of claim 33, wherein the interaction of the components of a sample with the expression array is measured by multi-dimensional spectroscopy utilizing ion mobility and time of flight mass spectroscopy for the detection of biological or chemical products formed as the result of the interaction of at least one component of the sample with proteins expressed from specific sites on the protein expression array.

47. A method for the detection of chemical or biological components immobilized on a solid phase by multidimensional spectroscopy (MDS) utilizing ion mobility and time of flight mass spectroscopy comprising the steps of:

(a) recovering at least a portion of a chemical or biological mixture immobilized on a solid substrate as an electrospray;

(b) directing the electrospray to an ion mobility chamber which separates the constituents of the directed electrospray by size, ionic charge, and shape; and

(c) analyzing the separated constituents which emerge from the ion chamber by time-of-flight spectroscopy.

48. The method of claim 47, wherein the immobilized components are immobilized as an array.

49. The method of claim 47, wherein the array comprises a microchip format.

50. The method of claim 47, wherein the array comprises an array of protein expression systems or products thereof.

51. Computer readable media comprising software code for performing the method of claim 47.